

Short Communication

Radiosensitivity in Fanconi's anemia patients

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Abstract

The risks of radiation therapy in patients with Fanconi's anemia who have cancer are not clear. Possible toxicity was reported in six of 14 patients: 1/1 with vaginal cancer, 4/10 with head and neck or esophageal cancer, and 1/3 with oral cancer following bone marrow transplant. Published by Elsevier Science Ireland Ltd.

Keywords: Fanconi's anemia; Radiation sensitivity; Head and neck cancer

1. Introduction

Patients with Fanconi's anemia (FA) have a high risk of cancer, and cancer treatment by chemotherapy or radiation is complicated because of the possibility of side effects due to the underlying defect in DNA damage response [1,6]. Marcou et al. [13] recently described marked clinical radiosensitivity in a 32-year-old female with FA and a tonsillar squamous cell carcinoma, and observed that in vitro tests of her fibroblasts did not predict the in vivo radiation sensitivity. This discrepancy is clinically significant, since in other DNA-repair disorders there does appear to be a correlation between in vitro and in vivo sensitivity to radiation [17]. The authors also stated that "clinical radiosensitivity has not previously been reported in FA patients". However, including their case, at least 14 FA patients who have received radiation therapy have been described in the medical literature, of whom six had complications that may have been related to the radiation.

2. Materials and methods

All cases of FA which have been reported in the literature were identified by systematic Medline searches using the terms 'Fanconi's anemia', 'inherited bone marrow failure', and 'aplastic anemia', supplemented by examination of citations in the references of published articles. This database was updated weekly using the same terms and Web of Science software [2]. Articles in languages which could not be read by the author were translated into English. All articles referring to FA cases were read carefully to deter-

mine whether cancer was mentioned. Cases who had FA and cancer, in whom radiation therapy was used for the cancer, comprise the population of interest for this review, which is completed through September 2001.

3. Results and discussion

Seventy-five cancers were reported in 64 FA patients who had not received a bone marrow transplant (BMT). Radiation therapy was used in 11 of these cases, one patient with vulvar cancer [23], and ten patients (seven females and three males) with head and neck or esophageal cancer (Table 1A) [4,8,10–13,16,18,19,22,23]. There were also eight FA cases who developed oral cancer at 3–14 years following BMT [3,5,7,9,14,15,20,21,24]; three of these patients received radiation for their tumors (Table 1B) [3,5,14,20].

In the only case of vulvar cancer treated with radiation, among a total of eight vulvar cancer cases, there was a severe moist skin reaction after 31 Gray (Gy) [23].

Radiation doses were reported in six of the untransplanted patients with head and neck or esophageal cancer, and ranged from 3.2 to 80 Gy (Table 1A). One female patient with cancer of the tongue and submandibular region had radiation mucositis after treatment with 3.2 Gy [12], while another female had radiation mucositis and ulceration of the hard palate and tonsil after 34 Gy [13]. A male patient with cancer of the upper esophagus died during the radiation period from laryngeal edema and pneumonia after receiving 70 Gy [10]. Another male patient with gingival cancer had local bleeding reported after receiving 80 Gy [11]. By contrast, a female tolerated 32.5 Gy 'very well' for cancer

Table 1
FA cancer patients and radiation therapy^a

No.	Age (yrs)	Sex	Cancer (All SCC)	Radiation Dose (Gys)	Complication	Status	Reference
(A) No BMT							
1	27	F	Vaginal	42.5	Severe moist skin reaction	D 3 mo	23
2	26	F	Middle esophagus	NS	None mentioned	D 4 mo	4
3	17	F	Mandible	68	None mentioned	D 3 mo	22
4	22	M	Gingiva	NS	None mentioned	A 10 mo	16
5	26	M	Cervical esophagus	70	Laryngeal edema	D during radiation	10
6	23	F	Tongue	NS	None mentioned	D 4 yrs	8
7	20	F	Middle esophagus	NS	None mentioned	D 2 mo	18
8	14	M	Gingiva	80	Local bleeding	D 6 mo	11
9	29	F	Post-cricoid	32.5	'Tolerated this very well'	D 12 mo	19
10	32	F	Tongue	3.2 ^b	Mucositis	D 9 mo	12
11	32	F	Tonsil	34	Mucositis, ulceration	A 3 mo	13
(B) BMT							
12	25, 29	F	Tongue, cheek	72	'Early severe mucositis' (cheek cancer treatment)	D 6 mo	3, 5
13	12	M	Tongue	NS	None mentioned	D 4 mo	20
14	18	F	Buccal	NS	None mentioned	D 3 mo	14

^a No., number; Age, at diagnosis of cancer; SCC, squamous cell carcinoma; F, female; M, male; yrs, years; mo, months; NS, not stated; A, alive; D, died.

^b Dose cited in manuscript.

of the posterior cricoid [19]. The other five reports did not mention outcome specifically related to the radiation.

A female FA patient who received a BMT at age 20 developed tongue cancer which was surgically removed at age 25, followed by cheek cancer at age 29 for which she received cisplatin, 5-fluorouracil, and 72 Gy local radiation, complicated by 'early severe mucositis'. Her transplant preparation consisted of 200 mg/kg of cyclophosphamide, without any radiation, but her post-BMT course was complicated by severe chronic graft versus host disease (GVHD) [3,5]. A male who had a BMT at age 6 after 6 Gy total abdominal radiation and did not have GVHD developed tongue cancer at age 12, and was treated with radiation of unstated dose, without mention of complications [20]. A female who had a BMT at age 9 after 6 Gy total body irradiation and who did have GVHD developed buccal cancer at age 18, for which she also received an unstated amount of radiation without mention of complications [14].

In summary, six of 14 FA patients for whom radiation was used to treat cancer did develop complications that might be ascribed to the treatment. The only patient with vaginal cancer for whom radiation therapy was used developed a skin reaction. Four patients among ten without BMT who had cancer of the head and neck or esophagus were reported to have laryngeal edema, local bleeding, mucositis, and mucositis with ulceration. One of the three patients who had received a BMT had mucositis from radiation therapy; this was the patient whose BMT preparation had not included radiation.

Most of the patients whose cancers were treated with radiation therapy died shortly thereafter, at 3 months for the patient with vaginal cancer, 3–12 months for eight of

the untransplanted ten patients with head and neck or esophageal cancer, and 3–6 months for all three of the post-BMT oral cancer patients. The only survivors were two untransplanted patients with oral cancer who were alive at 3 and 10 months following treatment with radiation. Although radiation therapy may be blamed for the outcomes, the poor survival may be a reflection of the advanced stage of the tumors for which definitive surgery was inadequate and radiation was required. However, in some cases radiation toxicity precluded completion of the therapeutic courses.

The number of published cases of solid tumors in FA [2] is small, the types of tumors vary (although the majority are head and neck or esophageal, followed by gynecological), the tumor sizes range from small and localized to large and metastatic, and the types of therapy are diverse. Thus, there is insufficient evidence to guide management of individual cases. It would appear prudent to use surgical intervention as much as possible, and to be concerned about choices of chemotherapy agents or radiation fields and doses in the context of a DNA-repair disorder. The importance of cancer surveillance to identify precancerous lesions or early malignancies seems clear, although currently of only theoretical merit in these high risk patients. Publication of additional case reports or series should be encouraged, in order to gather sufficient information to guide more specific recommendations in the future.

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